REMARKS

Reconsideration of the present application is respectfully requested in view of the above amendments and the following remarks. Claims 1-55 are pending; claims 1-21 are currently under examination and claims 22-55 are withdrawn. Without acquiescence, claim 4 is amended to particularly point out and distinctly claim certain embodiments of Applicants' invention. No new matter has been added by this amendment. Support for this amendment can be found in the claims as originally filed (*see, e.g.,* original claim 5).

RESTRICTION REQUIREMENT

The Examiner has made the Restriction Requirement final, asserting that even if Wang *et al.* teach away from the remanent magnetic particles of the instant claims, then the references cited in the instant Action teach such magnetic particles. Essentially, the Examiner asserts that the instant claims do not satisfy the requirements of Unity of Invention.

As previously made of record, Applicants respectfully disagree and submit that claims 1-55 share at least one special technical feature that distinguishes them over Weitschies *et al.* (U.S. Patent No. 6,027,946), Tan (U.S. Patent No. 6,548,264), and Rohr (U.S. Patent No. 5,445,970), whether in view of Nelson *et al.* (U.S. Patent No. 5,962,641) or otherwise. For instance, as discussed below, Applicants submit that none of these references, alone or in combination, teach or suggest a magnetic particle, as presently claimed, with the required specificity to be anticipatory under section 102, or obvious under section 103.

Therefore, even though Applicants recognize that the Restriction Requirement has been made final, Applicants respectfully submit that claims 1-55 satisfy the requirements of Unity of Invention under PCT Rule 13.2, and provide these remarks to preserve their right to petition for reconsideration and withdrawal of that requirement.

REJECTIONS UNDER 35 U.S.C. § 112, SECOND PARAGRAPH, INDEFINITENESS

Claims 1-21 stand rejected under 35 U.S.C. § 112, first paragraph, for alleged indefiniteness. First, the Examiner asserts that claim 1 is confusing, alleging that it is unclear how the "particle" in line 3 can aggregate, mainly because it already has a matrix that promotes

disaggregation. The Examiner also asserts that claim 5 lacks antecedent basis for the recitation "the ferromagnetic metal oxide," and asserts that the recitation "substantially spherical" in claim 1 is unclear.

Applicants traverse this rejection and submit that the instant claims are clear. A claim is clear under 35 U.S.C. § 112, second paragraph, if it defines the patentable subject matter with a ***reasonable*** degree of particularity and distinctness, mainly in view of the specification and the understanding of persons skilled in the art. *See* M.P.E.P. § 2173.02. Also, it is kindly submitted that some latitude in the manner of expression and the aptness of terms should be permitted by the Examiner. *Id.*

Applicants submit that claim 1 is reasonably clear to persons skilled in the art. For instance, merely by way of background, Applicants have discovered that the combination of remanent magnetic materials and matrix materials with functional groups on their surface promotes the disaggregation of particles that would otherwise form aggregates in solution. From this discovery, the property of remanence, previously thought to be undesirable in magnetic particle applications, can be utilized to confer advantageous properties on the magnetic particles. It is believed that this feature is clear to persons skilled in the art upon reading the instant disclosure.

As is clear from the first line of claim 1, the magnetic particles comprise two components: a magnetic material, and a matrix material. Claim 1 further specifies that the magnetic material is remanent upon exposure to a magnetic field, such that the particles form aggregates when suspended in a liquid phase, *i.e.* the remanence of the magnetic material must be sufficient to cause the particles to form aggregates. In this manner, the features of the magnetic material are defined, in part, by its ***ability*** to form aggregates in liquid phase.

Then, the matrix material is specified by the claim as having a surface comprising functional groups that ***promote*** disaggregation of the particles in the present of a liquid phase. In this manner, the matrix material is defined, in part, by its ***ability*** to promote disaggregation of a magnetic material that would otherwise form aggregates in the liquid phase. Given this understanding, which is readily apparent from the instant disclosure (*see, e.g.,* page 4, second full paragraph), Applicants believe that there is no conflict between the definition of the magnetic

material and the definition of the matrix material within claim 1, and, thus, submit that claim 1 is ***reasonably*** clear.

As to claim 5, Applicants note that claim 4 has been amended to recite, in pertinent part, "wherein the magnetic material comprises a ferrimagnetic metal oxide," thereby providing explicit antecedent basis for the recitation "the ferromagnetic metal oxide" in claim 5.

As to claim 8, Applicants submit that the recitation "substantially spherical" is reasonably clear to persons skilled in the art. For instance, such persons would understand this recitation to encompass spherical (*i.e.,* perfectly round) particles and spheroidal particles, or particles that are shaped like a sphere but are not perfectly round, such as an ellipsoid that is generated by revolving an ellipse around one of its axes.

In view of the amendments and remarks herein, Applicants submit that the instant claims satisfy the requirements of definiteness under 35 U.S.C. § 112, second paragraph, and respectfully request withdrawal of this rejection.

REJECTIONS UNDER 35 U.S.C. § 102

A. Claims 1-9, 11, and 13-19 stand rejected under 35 U.S.C. § 102(b) for alleged lack of novelty over Weitschies *et al.* (U.S. Patent No. 6,027,946). The Examiner alleges that Weitschies *et al.* disclose a magnetic particle of ferromagnetic or ferrimagnetic material that also comprises a matrix/shell with functional groups, such as aldehyde and thiol.

Applicants traverse this rejection and submit that the instant claims satisfy the requirements of novelty over Weitschies *et al.* In particular, Weitschies *et al.* fail to fairly disclose, with the degree of required specificity, a magnetic particle comprising a magnetic material ***which is remanent upon exposure to a magnetic field***, such that the particles form aggregates when suspended in the liquid phase in the absence of a magnetic field, and a matrix material which has a surface comprising functional groups which promote disaggregation of the particles in the presence of a liquid phase.

Weitschies *et al.* fail to disclose each feature of the instant claims with the requisite degree of specificity to be anticipatory under section 102. Mainly, and in contrast to the instant claims, Applicants respectfully submit that this reference teaches the preferential use of

superparamagnetic material, *i.e.,* material that is ***not remanent*** upon exposure to a magnetic field. Specifically, Weitschies *et al.* teach a method for magnetorelaxometric quantitative detection of analytes in liquid and solid phases that involves applying an external magnetic field to magnetic particles bound to a target, and measuring the relaxation time of the particle/target molecule complexes. However, it is believed that this method involves the use of ***superparamagnetic*** particles to bind target molecules. Indeed, as discussed in column 3, lines 20 to 41 of Weitschies *et al.*, an important principle of this method is that after the external magnetic field is turned off the magnetization of the particles relaxes ***within the measuring time*** by (i) Brownian relaxation or extrinsic superparamagnetism, and (ii) Neelian relaxation or intrinsic superparamagnetism. To obtain useful measurements, this method requires the magnetic particles to have a measurable Neelian relaxation over a relatively short time after the magnetic field is switched off. Hence, by requiring short Neelian relaxation times, the magnetic particles of Weitschies *et al.* do not have significant remanence, *i.e.,* they are essentially ***superparamagnetic***, because from a practical perspective, remanence would interfere with the measurements described therein.

In contrast, Applicants submit that the magnetic particles of the instant claims, which are remanent upon exposure to a magnetic field and form aggregates when suspended in a liquid phase in the absence of a magnetic field, would necessarily have Neelian relaxation times on the order of several months, even several years, making them different than the preferred particles of Weitschies *et al.* Given this inherent difference, which would render the instant particles unsuitable for the methods of Weitschies *et al.*, Applicants submit that the particles of Weitschies *et al.* do not fairly anticipate the subject matter of claim 1.

Applicants, therefore, submit that the instant claims satisfy the requirements of novelty over Weitschies *et al.*, and respectfully request withdrawal of this rejection under 35 U.S.C. § 102(b).

B. Claims 1-5, 7-18, and 21 stand rejected under 35 U.S.C. § 102(e) for alleged lack of novelty over Tan *et al.* (U.S. Patent No. 6,548,264). The Examiner asserts that Tan *et al.* teach a silica-coated nanoparticle, comprising a magnetic core of ferrimagnetic

material and a polymeric shell. The Examiner also asserts that the polymeric shell may be functionalized with a carboxylate group or an amine group.

Applicants traverse this rejection and submit that the instant claims satisfy the requirements of novelty over Tan *et al.* As above, Applicants submit that Tan *et al.* fail to teach each feature of the instant claims with the required degree of specificity to be anticipatory under section 102.

Tan *et al.* do not explicitly disclose a particle having ***both*** the required magnetic material and the required matrix material. At best, the disclosure of Tan *et al.* relates generally to the field of nanoparticles and methods of making nanoparticles, and discloses nanoparticles for use in a large variety of different fields, including semiconductor particles, dye-doped particles, pigment particles, *etc.*, as well as magnetic particles. Thus, it is only in a few variations that Tan *et al.* disclose particles with cores that can be magnetic (see column 2, lines 27 to 29).

In light of this limited disclosure on magnetic particles, Applicants' review of Tan *et al.* suggests that the Examples in this reference, at best, relate to the use of ***superparamagnetic*** material. However, in contrast to the magnetic material of the instant claims, superparamagnetic material is not remanent. Hence, in order to arrive at the instant magnetic particles, persons skilled in the art would have to start with a non-preferred material (*i.e.,* remanent material), and also select a matrix material comprising functional groups that will promote disaggregation of the particle in the liquid phase. But Tan *et al* make no mention of functional groups to promote disaggregation of the particles in the liquid phase. Indeed, it is respectfully submitted that persons skilled in the art would understand the functional groups of Tan *et al.* to be used in binding a secondary ligand.

In view of the above, it is respectfully submitted that persons skilled in the art would have to pick and choose among a large number of general features to arrive at the instant magnetic particles from the disclosure of Tan *et al.* Applicants submit that this situation is analogous to that of chemical arts, in which a compound is not specifically named, but instead it is necessary to select portions of teachings within a reference and combine them, *e.g.*, select various substituents from a list of alternatives given for placement at specific sites on a generic

chemical formula to arrive at a specific composition. In such cases, anticipation can only be found if the classes of substituents are sufficiently limited or well-delineated. *See Ex parte A*, 17 U.S.P.Q. 2d 1716 (Bd. Pat. App. & Inter. 1990). Here, Applicants submit that the substituents of Tan *et al.* are not sufficiently defined or well-delineated to arrive at a specific magnetic particle comprising a magnetic material that is remanent upon exposure to a magnetic field, in combination with a matrix material comprising functional groups which promote disaggregation of the particles in the presence of a liquid phase, as presently claimed.

Accordingly, Applicants submit that the instant claims satisfy the requirements of novelty over Tan *et al.*, and respectfully request withdrawal of this rejection under 35 U.S.C. § 102(e).

C. Claims 1-19 and 21 stand rejected under 35 U.S.C. § 102(b) for alleged lack of novelty over Rohr (U.S. Patent No. 5,445,970). The Examiner asserts that Rohr teaches a magnetic label comprising a ferromagnetic or ferrimagnetic core that is dispersed in a polymeric matrix, and that may comprise functional groups, such as aldehydes.

Applicants traverse this rejection and submit that the instant claims satisfy the requirements of novelty over Rohr. In particular, Rohr fails to fairly disclose, with the degree of required specificity, a magnetic particle comprising a magnetic material ***which is remanent upon exposure to a magnetic field***, such that the particles form aggregates when suspended in the liquid phase in the absence of a magnetic field, and a matrix material which has a surface comprising functional groups which promote disaggregation of the particles in the presence of a liquid phase.

Rohr fails to disclose each feature of the instant claims with the requisite degree of specificity to be anticipatory under section 102. Mainly, and in contrast to the instant claims, Applicants respectfully submit that this reference teaches the preferential use of ***superparamagnetic*** material, *i.e.,* material that is ***not remanent*** upon exposure to a magnetic field. Specifically, Rohr discloses a magnetically-attractable material as a detectable label in binding assays. As explained in column 2 lines 45 to 58, the magnetic label is subjected to a magnetic field and the label displays a resultant force or movement. The extent of the force or

movement is modulated by an analyte that may be present in the test sample, and the effect of the magnetic field on the magnetically-attractable label can be used as a measure of the presence or amount of an analyte in a test sample. Accordingly, it is apparent to persons skilled in the art that this method works in a manner akin to the method of Weitschies *et al*, described in section A above, and, thus, focuses mainly on the use of ***superparamagnetic*** particles.

In contrast, Applicants submit that the magnetic particles of the instant claims, which are remanent upon exposure to a magnetic field and form aggregates when suspended in a liquid phase in the absence of a magnetic field, are different than the preferred particles of Rohr, because the instant particles are not superparamagnetic. Further, Rohr does not specifically teach that functional groups may be added to remanent magnetic materials to promote disaggregation of the particles in a liquid phase. Indeed, the limited disclosure of functional groups relates to the attachment of further binding members, which would interfere with this purpose. Given these differences, which would likely render the instant particles unsuitable for the methods of Rohr, Applicants submit that the particles of Rohr do not fairly anticipate the subject matter of claim 1 and those that depend therefrom.

Applicants, therefore, submit that the instant claims satisfy the requirements of novelty over Rohr, and respectfully request withdrawal of this rejection under 35 U.S.C. § 102(b).

REJECTIONS UNDER 35 U.S.C. § 103

Claim 20 stands rejected under 35 U.S.C. § 103(a) for alleged obviousness over Weitschies *et al.* or Tan *et al.* or Rohr in view of Nelson *et al.* (U.S. Patent No. 5,962,641). The Examiner relies on Weitschies *et al.* or Tan *et al.* or Rohr as discussed in the section 102 rejections above, but agrees that these references fail to teach or suggest a target that comprises a metal and an affiant that comprises a chelator for the metal. The Examiner, however, asserts that Nelson *et al.* teach the use of several different metal chelating ligands for immobilized metal ion affinity chromatography to purify proteins, and also disclose a metal chelating complex for purifying recombinant proteins. The Examiner then asserts that it would have been obvious to use an appropriate binder for the analytes being detected, such as the chelator of Nelson, because

Weitschies *et al.* or Tan *et al.* or Rohr are alleged to require a binder/structure specific substance on their nanoparticles.

Applicants traverse this rejection and submit that the instant claims satisfy the requirements of non-obviousness over the cited references. In particular, Applicants submit that the Examiner has not established a *prima facie* case of obviousness with respect to the presently claimed subject matter (*See In re Mayne*, 104 F.3d 1339 (Fed. Cir. 1997) (The USPTO has the burden of showing a *prima facie* case of obviousness). The Examiner must at a minimum demonstrate that the combined references teach or suggest all the claim features, and even assuming, *arguendo*, that the combination of references teaches each claim feature, the Examiner must provide an explicit, apparent reason to combine these features in the fashion claimed by the Applicant with a reasonable expectation of success. *See KSR v. Teleflex, Inc.,* No. 04-1350 at 4, 14 (U.S. Apr. 30, 2007) ("A patent composed of several elements is not proved obvious merely by demonstrating that each element was, independently, known in the prior art").

In the present case, the Examiner has provided no technically sound, apparent reason why a person skilled in the art at the time of filing would have had any reasonable expectation of success in arriving at the claimed magnetic particles. The deficiencies in Weitschies *et al.* or Tan *et al.* or Rohr are discussed above (*see* Applicants' response to the § 102 rejections). Indeed, by focusing on the use of superparamagnetic materials, or materials that ***do not have remanence***, it is respectfully submitted that these references ***teach away*** from the magnetic particles of the instant claims, which are remanent upon exposure to a magnetic field such that the particles form aggregates when suspended in a liquid phase in the absence of a magnetic field. Moreover, none of these references provide any apparent reason to use a matrix material that comprises functional groups to ***promote disaggregation*** of the particles in the presence of a liquid phase, nor do they provide any reasonable expectation that this effect can be achieved by combining such matrices with remanent magnetic materials. Instead, Rohr, at best, teaches that functional groups are to be added to facilitate attachment to a further binding member. However, even assuming, *arguendo*, that the functional groups of Rohr are otherwise capable of promoting disaggregation in the liquid phase, they would be covered by the binding member and unable to fulfill this function. Hence, these references, alone or in combination, fail

to teach or suggest each feature of the instant claims, and further fail to provide any apparent reason to arrive at the presently claimed subject matter with a reasonable expectation of success.

With respect to claims 1-19 and 21, Nelson *et al.* do not remedy the deficiencies in any of Weitschies *et al.* or Tan *et al.* or Rohr, because this reference is entirely silent on the use of magnetic particles. With respect to claim 20, Nelson *et al.* further fail to provide any apparent reason to target metal ions by attaching a chelator to the instant magnetic particles, let alone do they provide a reasonable expectation of success in that endeavour. To the contrary, the use of metal chelators in protein-based affinity chromatography is not pertinent to their use in magnetic particles, and on its own provides no reasonable expectation that the use of chelators can be successfully adapted to magnetic particles – an entirely different technology with entirely different technical requirements. In this regard, it is kindly submitted that the Examiner's line of reasoning is insufficient to establish obviousness, since, in the absence of Applicants' disclosure, the Examiner has provided no technical evidence or reasoning to support the successful use of metal chelators on magnetic particles. *See KSR v. Teleflex, Inc.* at 14, citing *In re Kahn,* 441 F.3d 977, 988 (Fed. Cir. 2006) ("[R]ejections on obviousness grounds cannot be sustained by mere *conclusory statements*; instead, there must be some articulated reasoning with some rational underpinning to support the legal conclusion of obviousness.") (emphasis added).

Given these deficiencies, as detailed herein, Applicants submit that the cited references *in combination* fail to provide the requisite motivation and reasonable expectation of success in arriving at the presently claimed magnetic particles. In particular, since none of the references even remotely suggest magnetic particles capable of binding a target substance, which comprise a magnetic material and a matrix material, wherein the magnetic material is remanent upon exposure to a magnetic field such that the particles form aggregates when suspended in a liquid phase in the absence of a magnetic field, and the matrix material has a surface comprising functional groups which promote disaggregation of the particles in the presence of a liquid phase (*see* claim 1), let alone do they teach such particles that comprise a metal chelator for targeting a metal (*see* claim 20), the Examiner lacks the required technical basis to assert that the presently claimed methods are rendered obvious by the combination of references.

Applicants submit that the instant claims satisfy the requirements of non-obviousness under 35 U.S.C. § 103(a), and respectfully request reconsideration and withdrawal of the obviousness rejection to the claims.

Applicants believe that all of the claims in the application are allowable. Favorable consideration and a Notice of Allowance are earnestly solicited.

The Director is authorized to charge any additional fees due by way of this Amendment, or credit any overpayment, to our Deposit Account No. 19-1090.

Respectfully submitted,

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